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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,718	11/30/2000	Julian Van Erlach	XILL-3095	4074

5409 7590 09/13/2002

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EXAMINER	
PASS, BARRY	
ART UNIT	PAPER NUMBER
3737	

DATE MAILED: 09/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/727,718	Applicant(s) ERLACH ET AL.	
	Examiner Barry Pass	Art Unit 3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-19* is/are rejected.

7)☒ Claim(s) *16 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *26 July 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Drawings

1. The corrected substitute drawings were received on July 29, 2002. These drawings are accepted

Specification

2. The examiner's objections to the use of the term "NMR" (nuclear magnetic resonance) and the typographical error relating to Table 1 has been overcome by the applicant's amendment to the specification.

Claim Objections

3. Claims 16 and 17 are objected to because of the following informalities: in the first line "the step of chemically modifying..." lacks sufficient antecedent basis. Appropriate correction is required.

Double Patenting

4. Claims 1-9 and 11-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting, set forth in *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993), as being unpatentable over claims 1-17 of the inventive entity's copending Application No. 09727749 and over claims 1-14 of the inventive entity's copending Application No. 09/727,716. Although not all of the conflicting claims are identical, there is duplication and the remaining claims are not patentably distinct from each other because the broader claims of this application, which teach inserting a nanodevice into a fluid stream in the body, location of the nanodevice intra- or extracellularly, incorporating a microcircuit in the nanodevice, detection of the nanodevice, and facilitating binding of the nanodevice to target molecules anticipate and, in part, duplicate the more specific invention of a nanodevice to monitor a bodily condition disclosed in Application No. 09727749 and the more specific invention of methods for attaching a nanodevice to a cell disclosed in Application No. 09/727,716.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. The amended claims 9, 14 and 18 recite the limitation "the step of selecting" in the first line. There is insufficient antecedent basis for this limitation in the claim.

Examiner accepts changes to claims 3-8, 11-13 and 19 and removes rejections under this statute.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

8. Claims 1, 2, 4, 6, 7 and 15 are rejected under 35 U.S.C. 102(e) as anticipated by Vo-Dinh US 6,219,137 or, in the alternative, under 35 U.S.C. 103(a) as obvious over Vo-Dinh.

9. Referring to claims 1 and 7 Vo-Dinh discloses in column 2, lines 37-38 delivering nanoprobes inside organisms.

10. Referring to claim 2 Vo-Dinh discloses in the abstract injecting nanoprobes into cells. In addition, in column 2, lines 37-39 and column 5, lines 65-68, and column 6, lines 1-22, Vo-Dinh discloses methods for delivering nanoprobes inside a cell.

11. Referring to claim 4 Vo-Dinh discloses in column 5, lines 65-68, and column 6, line 1, inserting nanoprobe materials into a cell by micro injector.

12. Referring to claim 6 Vo-Dinh discloses in column 2, lines 33-37, a nanoprobe as a detector for toxic chemicals and other biological indicators.

13. Referring to claim 15 Vo-Dinh discloses in column 2, lines 35-41, delivering a nanoprobe into an organism for extracellular diagnosis.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. In the alternative, claims 1, 2, 4, 6, 7 and 15 are rejected under 35 U.S.C. 103(a) as obvious over Vo-Dinh.

17. Referring to claim 1 and 15, Vo-Dinh discloses in column 2, lines 18-41, delivering nanoprobes inside organisms, detecting bodily indicators, and intracellular and extracellular diagnosis by the nanoprobes. Vo-Dinh does not teach delivering the nanoprobe into a fluid stream within a body. However, it would have been obvious to someone of ordinary skill in the art at the time of the invention that the methods disclosed by Vo-Dinh for delivering nanoprobes into an organism for medical diagnosis would include the capability of inserting the nanoprobes into a fluid stream of a body if that stream is in a blood vessel. Also, it is well known in the art that the extracellular environment recited by Vo-Dinh contains streams of fluids. Referring further to claim 15, Vo-Dinh discloses in column 2, lines 35-41, delivering a nanoprobe into an organism for extracellular diagnosis.

18. Referring to claim 2 Vo-Dinh discloses a method of insertion as recited in claim 1; in the abstract teaches injecting nanoprobes into cells; in column 2, lines 37-39 and column 5, lines 65-68 and column 6, lines 1-22, Vo-Dinh teaches methods for delivering nanoprobes inside a cell.

19. Referring to claim 4 Vo-Dinh discloses a method of insertion into a cell as recited in claims 1 and 2, and teaches in column 5, lines 65-68 and column 6, line 1 inserting nanoprobe materials into a cell by micro injector.

20. Referring to claim 6 Vo-Dinh discloses a method of insertion as recited in claim 1 and in column 2, lines 33-37 a nanoprobe as a detector for toxic chemicals and biological indicators.

21. Referring to claim 7 Vo-Dinh discloses a method of insertion as recited in claim 1. It would have been obvious to someone of ordinary skill in the art at the time of the invention that insertion into organism as described by Vo-Dinh is equivalent to insertion into a biological member as described in the invention.

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country. more than one year prior to the date of application for patent in the United States.

23. Claims 1, 2, 6, 7 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Merkle.

24. Referring to claims 1, 2, 7 and 15 Merkle discloses in section 4, last paragraph, nanodevices in the circulatory system that (section 5 second paragraph) circulate freely throughout the body and able to enter individual cells. Inherent to these disclosures is inserting a

nanodevice into the circulatory system and said devices located in any or all of the following milieus: blood vessels, interstitial spaces (extracellular) and intracellular.

25. Referring to claim 6, Merkle discloses in section 5 a nanodevice with a small computer able to determine the concentration of specific molecules, and able to receive broadcast instructions. These attributes necessarily include the limitations in the invention disclosed in claim 6.

Claim Rejections - 35 USC § 103

26. Claims 3,5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vo-Dinh. Vo-Dinh discloses a method of insertion into an organism or biological member as recited in claim 1. Further, in column 6, lines 1-22, Vo-Dinh teaches methods for delivering nanoprobes inside a cell. Vo-Dinh meets the limitations of claim 5 except that it does not specify a cell type. However, because different cell types were art-recognized equivalents at the time of the invention in regard to methods of inserting into a cell, one of ordinary skill in the art would have found it obvious to substitute one cell type for another for the purpose of inserting a nanoprobe into a cell to monitor intracellular environments.

27. Alternatively, claims 3, 5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vo-Dinh in view of Hadlaczky et al. US 6,077,697. Vo-Dinh discloses a method of

insertion into an organism or biological member as recited in claim 1. Further, in column 6, lines 1-22, Vo-Dinh teaches methods for delivering nanoprobes inside a cell as recited in claim 2. Vo-Dinh does not teach cell types. Hadlaczky et al. teach in column 5, lines 28-41, methods of inserting (including microinjection and electroporation) into cells. Hadlaczky et al. also teach cell types including cells from plants, insects, reptiles, amphibians, and mammals, stem cells, lymphocytes and neural cells. Accordingly, it would have been obvious to someone of ordinary skill in the art at the time of the invention that microinjection and other insertion techniques as taught by Vo-Dinh can be used on the cell types recited in the claims of the invention.

28. Claim 9, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Merkle in view of Peeters US Patent No. 6123819 or, alternatively, Vo-Dinh in view of Peeters.

29. Referring to claims 9 and 14 Merkle or, alternatively, Vo-Dinh teaches a nanodevice circulating or stationed in the body as recited in claim 1. Merkle or, alternatively, Vo-Dinh does not teach a substrate made of well-known semiconductor materials gallium arsenide, silicon, silicon oxides or germanium. Peeters, in the abstract, column 1, lines 14-1, and column 4, lines 14-18 and 41-45, teaches nanoelectrode arrays built with substrates comprised of silicon, germanium, gallium arsenide, or other semiconductors to detect, characterize and quantify single molecules in solution such as individual proteins, complex protein mixtures, DNA and other molecules for disease or for pre-disease diagnosis. It would have been obvious to one having ordinary skill in the art at the time of the invention was made that a nanodevice or microdevice in the body to detect and diagnose as taught by Merkle or Vo-Dinh could have a nanoelectrode

array of Peeters to detect, characterize and quantify single molecules in solution such as individual proteins, complex protein mixtures, DNA and other molecules for disease or for pre-disease diagnosis.

30. Referring to claim 11 Merkle or, alternatively, Vo-Dinh teaches a nanodevice circulating or stationed in the body as recited in claim 1. Merkle or, alternatively, Vo-Dinh does not teach a (oscillating) resonance type device. Peeters, in column 9, lines 45-46, and column 10, lines 1-19, teaches detection of resonance type nanoelectrode arrays. It would have been obvious to one having ordinary skill in the art at the time of the invention was made that a nanodevice or microdevice in the body to detect and diagnose as taught by Merkle or, alternatively, Vo-Dinh can be provided with any passive or active function within the capabilities of nanoelectrodes and, in particular, can have that array constructed as a resonance device to enable detection.

31. Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Merkle in view of Østensen et al. US Patent No. 6,375,931 or, alternatively, Vo-Dinh in view of Østensen et al.

32. Referring to claim 12 Merkle or, alternatively, Vo-Dinh teaches a nanodevice inserted and within a body as recited in claim 1. Merkle or, alternatively, Vo-Dinh does not teach detecting the device by magnetic resonance. Østensen et al., teach in column 5, lines 53-67,\ and column 18, lines 41-45, micro- and nanoparticles circulating in a body and detectable by magnetic resonance for medical diagnosis. It would have been obvious to one having ordinary

skill in the art at the time of the invention was made that a nanodevice or microdevice inserted and within in a body as disclosed by Merle or, alternatively, Vo-Dinh can be a device detectable by the magnetic resonance techniques well-known in the art of nuclear magnetic resonance, electron spin resonance, and electron paramagnetic resonance (EPR).

33. Referring to claim 13 and 14 Merkle, or, alternatively, Vo-Dinh, and Østensen et al. teach a nanoprobe detectable by magnetic resonance as recited in claims 1 and 12. Merkle, or, alternatively, Vo-Dinh, and Østensen et al. do not teach molecules or compounds detected by EPR. It would have been obvious to one having ordinary skill in the art at the time of the invention was made that a nanodevice or microdevice inserted and within in a body as disclosed by Merle or, alternatively, Vo-Dinh and able to respond to EPR detection would incorporate substances well-known in the art to respond to EPR detection such as odd electron molecules or any of the well-known paramagnetic substances recited in claim 13, or an organic free radical as recited in claim 14.

34. Claims 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Merkle or, alternatively, Vo-Dinh as applied to claim 15 above further in view of Schechter et al. US Patent No. 4,120,649.

35. Referring to claim 16 Merkle or, alternatively, Vo-Dinh teaches a nanodevice circulating or stationed in the body as recited in claim 15 but does not teach treatment of the circulating or stationary device to prevent immunologic response and prolong tissue retention. Schechter et al.

teach in the abstract the treatment of transplants with a compound to improve biological function by reducing antigenicity and prolonging retention by the host. It would have been obvious to one having ordinary skill in the art at the time of the invention was made to treat a nanodevice or microdevice inserted and within in a body as disclosed by Merle or, alternatively, Vo-Dinh with a compound to improve biological function by reducing antigenicity and prolonging retention by a body. Further, in regard to claims 17 and 18, it is well known in the art that organo hydroxyls, including ethylene glycol, reduce immune system response and increase retention by tissues.

36. Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Merkle or, in the alternative, over Vo-Dinh as applied to claim 15 above further in view of Dustin et al. Patent No. 5,071,964. Merkle or. in the alternative, Vo-Dinh teaches a nanodevice circulating in the body but does not teach addition of a lipid anchor, using an organo hydroxyl, to the circulating device to facilitate its attachment to cell membranes. Dustin et al. teach in the abstract the use of lipid anchors to enable the attachment of circulating micelles to a variety of target molecules on a cell. Further, it is well known in the art that organo hydroxyls (e.g. ethylene glycol) are used as cross-linking molecules that can be modified to have little effect on the chemistry of the molecules being linked. Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to provide a nanodevice or microdevice in the body with a lipid anchor to promote attachment of the device to a cell and thereby prolong its presence in a body and enhance its diagnostic or therapeutic function.

37. Alternatively, claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Merkle or, in the alternative, over Vo-Dinh as applied to claim 15 above further in view of Li et al. Patent No. 6,090,408. Merkle or, in the alternative, Vo-Dinh teaches a nanodevice circulating in the body but does not teach addition of a lipid anchor, using an organo hydroxyl, to the circulating device to facilitate its attachment to cell membranes. Li et al. teach in the abstract, column 14, lines 59-67, and column 15, lines 1-5, the use of ethylene glycol as a lipid anchor to enhance the attachment of circulating microparticles (liposomes) to reduce clearance by the reticuloendothelial system and thereby increase the medical effectiveness of the microparticles. Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to provide a nanodevice or microdevice in the body with a lipid anchor to promote attachment of the device to a cell and thereby prolong its presence in a body and enhance its diagnostic or therapeutic function.

Response to Arguments

38. The correction of objections to the drawings and specification is noted in this action.

39. The correction of claim rejections under U.S.C. 112(b) is noted in this action.

40. The issue of double patenting is re-addressed in this action.

41. In regard to claim rejections under U.S.C. 102(b) and U.S.C. 103(a) the examiner notes the applicant's objections to Merkle but maintains it is appropriate prior art. However, the examiner has introduced additional prior art as an alternative to Merkle.

42. The rejection of claims 1, 2, 6, 7, and 15 under U.S.C. 102(b) is re-addressed in this action.

43. The rejection of claims 3-5, 8-9, 11-14, and 16-19 under U.S.C. 103(a) is re-addressed in this action.

Conclusion

44. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Benjamin et al. US 4,793,825 teach injection of microparticles into the blood stream of animals to perform medical diagnosis and therapy. The devices carry signal processing means and integral battery for operating power. The surfaces of the devices are coated with a substance to promote adherence to target molecules.

Papisov et al. US 5,582, 172 teach injecting nanoparticles into an animal for diagnosis and therapy. The nanoparticles are labeled for detection by EPR and NMR, are coated with a molecule to promote linking with target tissues.

Jung et al. US 6,074,650 discuss in detail the use of cross-linking molecules and membrane anchors, and applies them to liposomes.

45. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barry Pass whose telephone number is (703) 305-0726. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marvin Lateef can be reached on (703) 308-3256. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0758 for regular communications and (703) 308-0758 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0873.

Barry Pass
August 30, 2002

Marvin M. Lateef
Supervisory Patent Examiner
Group 3709